RESEARCHUPDATE

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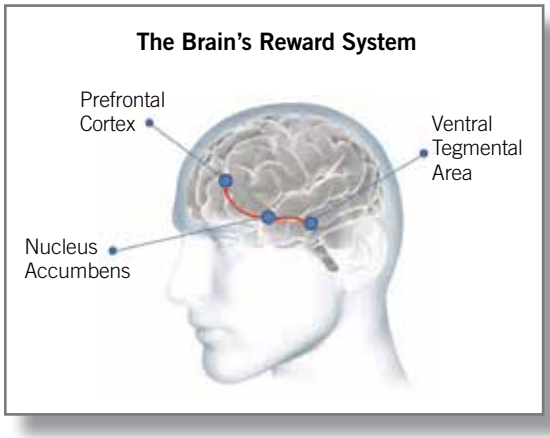
Research Update is published by the Butler Center for Research to share significant scientific findings from the field of addiction treatment research.

Drug Abuse, Dopamine, and the Brain's Reward System

Advances in neuroscience, psychology, and biology have shed light on the ways that long-term use of alcohol and other drugs change the brain to foster continued and chronic patterns of compulsive drug abuse. These efforts have not only helped redefine addiction as a disease but have increased our understanding of the underlying neurobiology that influences the progression from casual first-time use to chronic abuse that often leads to harmful, long-term consequences. The understanding of the effects of these substances on key brain areas throughout this progression has informed and guided behavioral and pharmacological treatments, further defining addiction as a *treatable* disease.

The Brain following Initial and Early Substance Use

Individuals use drugs of abuse for a variety of reasons, but the euphoric feelings and intense pleasure associated with being "high" are the most frequently reported.[1] It has long been established that this feeling is due to the drugs effect on brain areas that regulate and reinforce natural rewards that are vital to our existence, such as food and sex.[2] These brain areas, collectively referred to as the brain's reward system (or the mesolimbic dopamine system), are connected by neurons (i.e., brain cells) that originate in a structure deep within the brain called the ventral tegmental area. Dopamine released by the ventral tegmental area acts as a chemical messenger that signals the activation of neurons located in the nucleus accumbens, a structure often referred to the brain's "pleasure center" due to its influence on motivation and reward.[3] Researchers have demonstrated that activation of the nucleus accumbens allows us to predict whether something will be rewarding or pleasurable.[4] Animal and human studies have demonstrated that the nucleus accumbens activates when exposed to natural life-sustaining rewards, such as when food is presented while in a state of hunger.[5,6] Nearly all drugs of abuse increase dopamine in the nucleus accumbens, and they do so with greater efficiency and more prolonged effects than natural rewards.[7]



The Brain following Chronic and Long-Term Substance Abuse

The activation of the ventral tegmental area and the resulting flood of dopamine within the nucleus accumbens are the first steps of initial drug use that can eventually lead to the chronic and compulsive patterns that define drug abuse. Recent research with humans using the latest brain imaging technology has increased our understanding of the neurobiology underlying this important transition. Following repeated drug use that produces unnaturally high levels of dopamine within the reward system, the brain adapts by decreasing the number of receptors that dopamine specifically targets (i.e., dopamine receptors).[9] There are several types of dopamine receptors, and all are important to healthy brain function, but the one most consistently associated with drug abuse is the dopamine receptor called D2R.[9] Results from research using PET imaging have demonstrated significant reductions of D2R in the reward system of individuals with substance abuse problems.[9] Researchers reason that the reduction in D2R following long-term drug use can eventually result in a state of anhedonia, which is characterized by a lack of enjoyment in activities that were previously enjoyable such as socializing with friends and family or engaging in healthy non-drug-related activities.[10] These individuals may feel compelled to take drugs just to relinquish this anhedonic state and approximate normal reward system function.[7]

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THE HAZELDEN EXPERIENCE

Upon entering treatment many patients show signs of impaired cognitive function such as poor problem solving skills; however, these impairments improve during abstinence and treatment. Hazelden uses a comprehensive abstinence-based Twelve Step treatment approach that incorporates cognitive-behavioral and group therapy to promote recovery from the long-term consequences of drug abuse.

At the Butler Center for Research, studies are currently underway to assess cognitive processing of alcohol-related cues in individuals with alcohol dependence in hopes of better understanding the cognitive factors that influence vulnerability to relapse.

CONTROVERSIES & QUESTIONS

How long does cognitive impairment due to drug abuse last?

All drugs of abuse, when taken for extended periods of time, produce long-term dysfunction in the way the brain processes information, and the severity of the dysfunction is related to the frequency and duration of drug use. Over time, abstinence and active participation in treatment programs can drastically improve cognitive function impairments related to prolonged drug abuse.

Why are drugs more addictive than natural rewards?

Drugs of abuse can release approximately 2 to 10 times the amount of dopamine compared to natural rewards and are therefore more effective in stimulating the brain's reward system. The effects of drugs of abuse can also be immediate (e.g., when smoked or injected) and are longer lasting than the effects produced by behaviors that are naturally rewarding. The efficiency of drugs of abuse in activating the reward system results in strong motivation to continue to take drugs and a lack of motivation to engage in behaviors that are not drug related.

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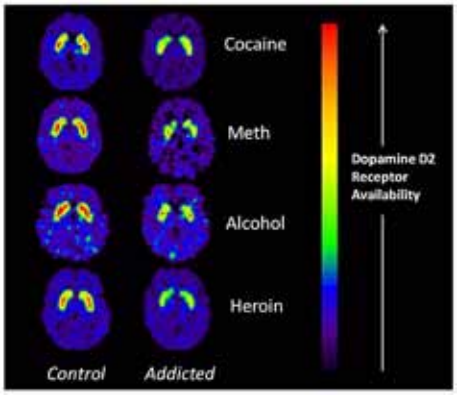
The reduction of D2R is associated with dysfunction of an additional structure in the brain's reward system. The prefrontal cortex is located at the forefront of the brain and, like the nucleus accumbens, its activation is modulated by the dopamine it receives from the ventral tegmental area.[11] However, unlike the nucleus accumbens, the role of the prefrontal cortex is to evaluate reward impulses and determine whether they are safe to pursue.[11] In a sense, the prefrontal cortex exerts parental control over the brain's reward system so that the rewards that are pursued are safe and beneficial to sustaining life. Research has shown that problems within the prefrontal cortex are associated with a lack of inhibitory control and forethought (i.e., impulsivity) in addition to poor decision making with regard to the long-term consequences of behaviors.[11] Researchers began investigating the role of the prefrontal cortex in drug abuse given the similarity between these maladaptive behaviors and the compulsive drug taking that occurs despite the resulting adverse consequences in individuals who have chronic substance abuse problems.[11]

Dopamine D2 Receptors are Lower in Substance Abusers



Source: NIDA, 2010

Results from imaging studies have demonstrated severe dysfunction in the prefrontal cortex of individuals with long-term substance abuse problems,[11] and more recent studies have shown that the magnitude of this dysfunction is correlated with substance abuse severity. Furthermore, evidence from structural imaging studies indicates that the material that primarily makes up the prefrontal cortex and is vital to its function (i.e., gray matter) is reduced by up to 20 percent in individuals with chronic substance abuse problems.[15, 16, 17, 18] Data indicate that the severity of gray matter reduction is associated with longer lifetime drug use and worse executive control problems.[13, 14] Current theories of substance abuse suggest that motivation to take a drug is initially inhibited by the prefrontal cortex due to the perceived adverse consequences; however, as drug use continues, the prefrontal cortex becomes less able to regulate activation of the reward system and drug use becomes compulsive despite the problems it may cause.[19]

Treatment Implications

Results from studies of the neurobiological effects of drugs have validated preexisting treatment methods and informed the development of new strategies to form a multipronged approach to the treatment of drug abuse. Intrinsic to this approach is a need to 1) decrease the reward value of drugs and increase the value of nondrug rewards, 2) weaken the drive that facilitates drug taking by abstaining from drug-related behaviors, and 3) strengthen the brains ability to control impulses to use drugs.[8] Evidence indicates that the brain is more resilient than previously thought and can recover from damage associated with long-term substance abuse. For example, the loss of D2R following heavy methamphetamine use can recover over long-term abstinence,[7] and active participation in cognitive behavioral therapy has been shown to increase gray matter volume in the prefrontal cortex.[20] Thus, the brain can recover from the detrimental and long-term consequences of drug abuse given time and treatment.

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The Butler Center for Research informs and improves recovery services and produces research that benefits the field of addiction treatment. We are dedicated to conducting clinical research, collaborating with external researchers, and communicating scientific findings.

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